RESPONSE

I. Status of the Claims

Claims 2 and 3 have been amended. Claims 2-3, 5 and 6 are therefore presently pending in the case. In an attempt to comply with 37 C.F.R. §1.121 and for the convenience of the Examiner a clean copy of the pending claims is attached hereto as **Exhibit A**.

II. Support for the Amended Claims

Claim 2 has been amended to further clarify the claim, and to recite the entire amino acid sequence. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 2 as originally filed and at page 4, lines 24-30.

Claim 3 has been amended to further clarify the claim, and to recite the entire amino acid sequence. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 3 as originally filed .

Amendments to Claims 2 and 3 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry, therefore, is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. § 101

Claims 2, 3, 5 and 6 are rejected under 35 U.S.C. § 101 because the claimed invention allegedly lacks patentable utility due to its not being supported by either a specific and/or substantial utility or a well-established utility. Applicants' respectfully disagree.

The Action discounts the real world economic value of the information provided by sequences of the present invention and states "such practices are directed to massive database evaluation and not to individual sequences, such as those claimed (Action at page 3 line 7-9). However, without the individual biologically validated sequences, such as provided by those of the present invention, genomic sequence information is of limited value. This is because only a small percentage of the genome (2-4%) actually encodes exons, which in-turn encode amino acid sequences. Thus, **not all human genomic DNA sequences** are useful in such gene chip applications, further discounting the Examiner's position that such uses are generic or that any DNA molecule will provide useful information. Thus, the present

claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

The Action also discounts Applicants further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the utility the present nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions, as described in the specification and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences (see evidence below). In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.*

(*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. The Action doubts the real world value of this information and states "such practices are directed to massive database evaluation and not to individual sequences, such as those claimed (Action at page 3 line 7-9). However, Applicants respectfully submit that without the individual biologically validated sequences, such as provided by those of the present invention, genomic sequence information is of limited value.

The Action also suggests that the use of the presently claimed polynucleotides, as in DNA chips, would be generic. Further, the Action seems to be requiring Applicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Applicants respectfully point out that knowledge of the exact function or role of the presently claimed sequence **is not required** to track expression patterns using a DNA chip. As set forth in Applicants First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. The claimed sequence provides a specific marker of the human genome, and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as described in the specification. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, as well as more recently issued U.S. Patent Nos. 5,837,832, 6,156,501 and 6,261,776. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful.

The Action also discounts Applicants assertion and evidence supporting the same, that the sequences of the present invention have specific utility in chromosome mapping, localizing the specific region of the human chromosome which encodes this gene. As evidence Applicants have provided evidence that the sequences of the present invention are the product of a gene encoded on human

chromosome 9. The three protein encoding exons are non-contiguously spread along a region of human chromosome 9 and contained within 2-3 different genomic clones: BC035124, BD027333, and AL355987. The interface between coding (exons) and non-coding regions (introns) of genomic sequence within this gene identifies functionally active intron/exon splice junctions. As the multiple exons encoding this protein are non-contiguous, clearly one would not simply be able to map the protein encoding regions that have been identified specifically by the sequences of the present invention, without knowing those specific sequences. Thus clearly the sequences of the present invention have utility in both chromosome mapping and the identification of functional intron/exon splice junctions.

For the reasons described above, the present invention clearly has specific, substantial, credible and well established utility. Therefore, Applicants submit that the rejection of claims 2,3,5 and 6 under 35 U.S.C. § 101 has been avoided and request that the pending rejection of the claims under 35 U.S.C. § 101 be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claims 2, 3, 5 and 6 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility, or alternatively, a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention. Applicants respectfully submit that as pending claims 2, 3, 5 and 6 have been shown to have "a specific, substantial, and credible utility" as detailed in the section above. Applicants therefore request that the rejection of claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claim 3 and new claims 5 and 6 are also rejected under 35 U.S.C. § 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Action maintains the rejection of Claim 3 and dependent claims 5 and 6, for recitation of the phrase "*the* amino acid sequence" which the Action alleges is vague. Applicants in no way agree, however in order to progress the case more rapidly toward allowance the claim has been revised to recite "the entire amino acid sequence". Thus, the rejection of Claim 3 and dependent claims 5 and 6 under 35 U.S.C. § 112 second paragraph has been avoided.

VI. Rejection of Claims under 35 U.S.C. § 102

Claims 2-3 and new claims 5 and 6 remain rejected under 35 U.S.C. § 102 as being anticipated by Xu. Applicants in no way agree with the present rejection, for the reasons stated in Applicants' prior response. However, solely in order to progress the case more rapidly toward allowance claims 2-3 have been revised to recite "the entire amino acid sequence". SEQ ID NO:52 of Xu (P/N 6,284,241) contains a 144 residue fragment of SEQ ID NO: 1 and therefore cannot encode the entire amino acid of SEQ ID NO:2, but only a 48 amino acid fragment thereof, and as such cannot properly anticipate the full-length molecules. Applicants therefore respectfully submit that Xu (P/N 6,284,241) does not properly anticipate claims 2 and 3 and dependent claims 5 and 6 under 35 U.S.C. § 102(e) and respectfully request withdrawal of the rejection.

VII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Smith have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

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Date

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